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(54) METHOD AND COMPOSITION FOR TREATING SEBORRHEIC DERMATITIS

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This invention relates to a method and composition for the treatment of seborrheic dermatitis in an aqueous isopropanolic or other suitable carrier and by using the composition as hereinafter described, dandruff can be controlled or eliminated.

The compound N,N-diethyl-m-toluamide is known and has been used as an insect repellant by the Armed Forces and others for that specific purpose for several years. The compound as usually prepared is 90 to 95% pure and is readily available commercially.

In accordance with the present invention it has been discovered that N,N-diethyl-m-toluamide is useful in the treatment of seborrheic dermatitis and related conditions such as seborrhea sicca capitis or pityriasis capitis. Thus, the present invention makes it possible to treat and control dandruff and the related scalp conditions. It has further been found that the N,N-diethyl-m-toluamide can be suitably incorporated into a carrier or vehicle which is preferably an aqueous isopropanolic liquid carrier or vehicle. The N,N-diethyl-m-toluamide is the active ingredient for dandruff control and is used in an amount ranging from about 5% to about 20% by volume of the composition. Good results have been obtained with 7% and excellent results have been obtained with 12%. In general, the composition is to be used in the minimum amount required for dandruff control and is employed daily for 1 to 3 weeks depending upon the severity of the condition of a particular patient and the responsiveness thereto of the condition being treated. In many instances it has been found that favorable results are obtained in about 1 week and that ordinarily it is not necessary to continue more than 3 weeks. Each time the composition is applied enough thereof is used to dampen the hair or saturate the scalp and it has been found by way of example that a 2 ounce container of the composition is enough to last for 2 weeks of treatment. The individual dosage applied to the hair and/or scalp is not critical and it is only necessary to use enough each time to dampen the hair or substantially saturate the scalp and after application of the composition, it has been found desirable to carry out fingertip massage for about one minute. The composition is intended to be used daily each morning, but may be applied as required for dandruff control. It will be

appreciated that in a given instance the amount used depends upon the amount of hair. Tests have been carried out with favorable results as hereinafter outlined and there were no adverse side effects.

Experience has shown that dandruff is often persistent and returns after weekly shampoos and regular hair grooming and is the result of a dermatitis, mainly seborrheic dermatitis, but also in some cases seborrhea sicca capitis or pityriasis capitis. Medications most commonly used to combat dandruff include sulfur, resorcinol, mercury, chrysarobin and coal tar. These have been found to have only limited value and are frequently accompanied by serious disadvantages. Sulfur is unsightly and may itself cause serious dermatitis. Resorcinol discolors hair and causes light and red hair to become greenish. Mercury is apt to be absorbed and is toxic. Chrysarobin is capable of producing renal irritation when applied to large areas or conjunctivitis if used adjacent the eyes. Coal tar is messy and potentially carcinogenic.

Clinical studies have been carried out in a variety of cases and have produced unusually successful results with no failures. In one such clinical study the amount of N,N-diethyl-m-toluamide was 7% and in another study the amount of active ingredient was 12%. The 7% clinical study was carried out on a group of 26 patients with severe intractable dandruff. There were 17 men and 9 women. Their average age was 39.4 years and the ages ranged from 21 to 54. In 16 cases the diagnosis was seborrheic dermatitis, in 6 cases the diagnosis was seborrhea sicca capitis and in 4 cases the diagnosis was pityriasis capitis. The patients had the condition from 1 to 9 years and on an average of 3.8 years. In most of these cases there was a considerable reduction of dandruff in the first week and the dandruff completely disappeared by the end of the second or third week. In 5 cases treatment was continued for 4 weeks before the dandruff was fully controlled. Successful results were obtained in 1 to 4 weeks averaging 2.6 weeks. In 18 cases or 69% the dandruff completely disappeared without recurrence during the period of observation. In 5 cases or 19% there was only slight recurrence of dandruff after 1 week. In 3 cases or 12% there was some recurrence of dandruff after 1 week, but considerably less than that prior to treatment. Favorable results were obtained in all 26

cases and in no case did the dandruff return in anywhere near its original severity. No irritation, itching or other side effect occurred in any case.

In the 12% clinical study there were 25 patients on whom a double-blind test was carried out, one composition being designated as Lotion A and the other as Lotion B. Neither the patient nor the physician knew which was which. Lotion A was the one containing 12% of active ingredient and it was made up as follows:

N,N-diethyl-m-toluamide	12 ml
Distilled water	38 ml
Isopropanol	50 ml
Perfume (perfume compound No. 30462 Fritzche Brothers)	up to 1.5 ml

In this double-blind study the 25 subjects were initially examined and evaluated as to the duration of the condition, the symptomatology and objective findings of their seborrheic dermatitis. The subjects were directed to continue to employ their usual practice of shampooing and washing. Lotions A and B were dispensed alternately in 2 ounce bottles and the subjects were instructed to apply the lotion to the scalp daily for a period of 2 weeks at the end of which time the subjects were evaluated both objectively and subjectively and then given another 2 ounce bottle of the same lotion to be used for an additional 2 weeks and at the end of the 4 week period they were again evaluated. The subjects were then placed on a rest period of approximately 3 weeks to avoid carry-over effects from the initial lotion and at the end of the 3 week rest period, they were given the alternate lotion which they used for a 2 week interval and at the end of this time the subjects were again evaluated and given another 2 week course of the same lotion. Thus, each subject used Lotion A and Lotion B for at least 4 continuous weeks with an approximately 3 week intervening rest period to avoid carry-over effects which might influence the proper evaluation of the alternatively used lotion. The age, sex, race and duration of disease are set forth in the following table:

TABLE I

Case No.	Initials	Age	Sex	Race	Duration of Complaint
1.	L.M.	17	F	C	1 Year
2.	C.D.	43	F	N	4 Years
3.	B.H.	17	F	C	2 Years
4.	B.W.	19	F	C	4 Years
5.	M.H.	15	M	C	2 Years
6.	L.T.	26	F	C	6 Months
7.	C.J.	42	F	N	2 Years
8.	T.S.	30	F	C	2 Months
9.	M.T.	42	F	C	26 Years
10.	M.McM.	30	F	C	2 Years
11.	S.B.	26	F	C	6 Years
12.	N.O'C.	37	F	C	4 Years
13.	M.E.	47	F	C	2 Months
14.	V.F.	36	F	C	6 Weeks
15.	P.H.	21	F	C	2 Years
16.	M.A.	38	F	C	1 Month
17.	B.H.	36	F	C	3 Years
18.	E.W.	43	F	C	1 Year
19.	S.L.	19	F	C	15 Months
20.	C.D.	29	F	C	6 Weeks
21.	B.L.	41	F	C	1 Year
22.	M.G.	33	F	C	3 Months
23.	M.B.	57	F	C	3 Years
24.	E.M.	46	F	C	2 Years
25.	H.K.	45	M	C	10 Years

The comparative evaluation of Lotion A versus Lotion B is set forth in the following table:

TABLE II

Case	Erythema	Scaling	Oiliness	Dryness	Crusting	Itching	Burning
1	A	A	B	None	A	A	None
2	A	A	B	Same	None	A	None
3	A	A	B	None	None	Same	None
4	A	A	B	None	A	A	None
5	A	A	B	None	None	Same	None
6	A	A	None	A	A	A	None
7	A	A	B	A	B	A	A
8	A	A	B	None	None	A	None
9	Same	A	None	A	A	A	A
10	A	A	Same	A	None	A	None
11	A	A	None	A	A	A	None
12	A	A	B	None	None	A	A
13	A	A	B	A	None	A	None
14	A	A	B	A	A	A	None
15	A	A	B	None	None	A	None
16	B	A	None	B	None	A	None
17	A	A	None	B	A	A	None
18	A	A	None	A	A	A	None
19	Same	A	B	A	A	A	None
20	A	A	A	Same	A	B	None
21	A	A	None	A	A	A	None
22	A	A	None	A	A	A	None
23	A	A	B	A	None	A	None
24	A	A	A	A	A	A	None
25	A	A	B	None	A	A	None

Symptomatology is improved to a greater degree with the lotion indicated. None signifies that the particular symptom was not a presenting complaint. Same signifies that both lotions had an equal effect.

It was found that in the 25 subjects with seborrheic dermatitis, Lotion A which contained 12% of N,N-diethyl-m-toluamide caused erythema to be decreased or eliminated in 22 or 88% of the cases as compared with only 4% for

Lotion B which was a placebo lacking the active ingredient. Scaling was eliminated in 18 cases and decreased in 7 cases with Lotion A, whereas with Lotion B there was decreased scaling in only 8 cases with 10 cases remaining unchanged and 7 cases becoming worse. Thus scaling was decreased or eliminated in 100% of the cases with Lotion A and in addition pruritus was markedly decreased or eliminated in 22 or 88% of the subjects with Lotion A, while only one improved with Lotion B. Some of the patients observed an increased oiliness with Lotion A, but this did not interfere with the effectiveness of the composition. Some subjects objected to the particular perfume, but this in inconsequential with respect to the efficacy of the composition.

Dermatologists recognize that seborrhea capitis and seborrheic dermatitis are important contributory causes of alopecia. Seborrhea in some form is considered as the most important local cause of premature alopecia ranging from 75 to 90% as an etiological factor. Dermatologists further recognize that seborrheic conditions recurring in later years are likely to become chronic, persistent and intractable. It was therefore most surprising and unexpected that the present invention was able to obtain such satisfactory results and this could not in any way have been predicted from existing knowledge of N,N-diethyl-m-toluamide itself which, while known as an excellent insect repellant, has not heretofore been known to be useful for the purposes of the present invention. N,N-diethyl-m-toluamide is readily available and has the empirical formula $C_{12}H_{17}NO$ with a molecular weight of 191.26. It is freely soluble in alcohols and for the purposes of the present invention, it is suspended or dissolved in any suitable carrier or vehicle but it has been found to be best and is therefore preferred to use the compound in the formulation above set forth with respect to the 12% clinical tests. Where a different amount of active ingredient is employed such as 7%, the amounts of water and alcohol are adjusted proportionately. It is further to be understood that while it has been found best to employ the active ingredient in aqueous isopropanolic solution, the invention is not limited thereto as the N,N-diethyl-m-toluamide can be incorporated in or combined with other carriers or vehicles whether liquid or semi-liquid such as conventional shampoos, hair rinses and hair tonics.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A method of treating seborrheic dermatitis which comprises applying to the hair or scalp periodically a sufficient amount of a composition to moisten the hair or substantially saturate the scalp and to control the dermatitis, which composition consists essentially of a carrier or vehicle in which is incorporated about 5 to 20% by volume of N,N-diethyl-m-toluamide based on the complete composition.

2. A method according to claim 5 in which the N,N-diethyl-m-toluamide amount to 12% by volume of the composition.

3. A method according to claim 5 in which the N,N-diethyl-m-toluamide amounts to 7% by volume of the composition.

4. A method of treating seborrheic dermatitis which comprises applying daily to the hair or scalp a sufficient amount of a composition to dampen the hair or substantially saturate the scalp for a period of 1 to 4 weeks, said composition being essentially composed of, per each 100 milliliters, 12 milliliters of N,N-diethyl-m-toluamide.

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